PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	Frequencies and ethnic distribution of ABO and RhD blood groups in China: a population-based cross-sectional study
AUTHORS	Liu, Jue; Zhang, Shikun; Wang, Qiaomei; Shen, Haiping; Zhang, Yiping; Liu, Min

VERSION 1 – REVIEW

REVIEWER	Paul Froom Tel Aviv University, Israel No Competing Interest
REVIEW RETURNED	17-Jul-2017

GENERAL COMMENTS	The paper is poorly presented. There are too many tables, some redundant. why do you need table 1 with the demographic details (what is the relevance of proportion of farmers for example).They certainly cannot make a case for policy based on the findings. The percentages should be limited to 1 point after the decimal place for clarity. The figure 3 is mis-labled.

REVIEWER	Rena Hirani Australian Red Cross Blood Service
REVIEW RETURNED	01-Aug-2017

GENERAL COMMENTS	The authors have described the ethnic distribution of ABO and Rh(D) type within the general Chinese population. This study would be valuable for the Chinese blood donor organisations to understand which ethnic groups they are mostly likely to encounter and how the blood groups would form part of this diversity. Overall the standard of writing is suitable, however some suggestions have been requested. Specific comments that need to be addressed have been annotated and attached in the file. Sections in yellow either need to be addressed, contain errors or a change has been made for the authors to consider from the original document. In summary Rhesus is no longer the accepted term under the ISBT guidelines. Also it should be stipulated which antigen is being analysed. Rh can refer to the D and CE systems as well as other systems. Since the CE was not analysed and can also result in Rh negative phenotypes with variable expressions in the community it should be stipulated that it was the Rh(D) group analysed. Acceptable nomenclature include RhD, Rh(D) or D. Whichever is chosen should be used consistently throughout where currently a

	number of them are used interchangeably. Similarly either the words 'negative' 'positive' should be used or the symbols not both. in the statistics analysis of the methods the confidence intervals used were not stated. If the aim of this study is to understand more about the ethic groups some more information on the demographic breakdowns would be useful in the results section. Proportions of females are missing as are the ethnic group male and female breakdowns. This could be added to table 1 briefly where the male proportion can be stated in brackets where the ethnic groups are shown. Table 2 and 3, the asterix for showing significance is not placed correctly. I believe the authors are trying to say that the proportion of A, B, AB and O is different between each group. i.e. are the authors trying to say that for example the difference the A blood group proportion between the Yi (33.95%) and Zhuang (25.19%) is statistically different or that for Zhuang the proportion of group O (41.81%), group B (27.49%), group A (25.19%) and group AB (5.5%) is statistically significant? For table 3 this is clearer in that the proportion of Rh(D) positive is significantly different to Rh(D) negative people in all ethnic groups. However it is clear that Uygur ethnicity is more significantly different to the other groups so perhaps the asterix should be placed next to that groups results. comment should be made whether Yi, Han and 'others' are significantly different from each other with regard to the proportion of Rh(D) negativity. figure 1 and 2 have the same information in different graphs and i don't think they are both necessary. I think figure 1 suffices. figure 3 the figure key is missing figure 4 please use the same orientation and organisation as used in figure 1 to prevent confusion for readers. the discussion needs a lot of work and is not very strongly concluding of the work conducted. The authors report the proportions of ABO and Rh(D) type for the ethnic groups but the text of putting them in context of other asian studies or against the caucasian populations is scattered throughout the discussion. This should be consolidated into one paragraph. the point of the publication from Australia on O Rh(D) negative blood use was that only a small proportion of O Rh(D) negative blood units were used in patients who required them (O Rh(D) negative recipients, trauma, obstetrics and neonates). Perhaps the authors would like to comment on that fact that since 98.98% of their population findings were Rh(D) positive individuals why this could not be applied to the blood donation sector in China. Why has the rate of O Rh(D) negative blood collections doubled from 2006 to 2012 when 98.98% of the population are Rh(D) positive. Are there plans and strategies to use the authors information to inform the clinical community of their findings and how they do not need to use O Rh(D) negative blood units. Although the information given does not include the willingness of the participants to donate, will this information be used to target blood donors specifically? I also did not understand the reference to blood groups and hereditary diseases as this cohort was not examined for this purpose. The authors mention that they did not analyse all the ethnic minorities 'due to the lack of relative information' can the authors please state what information is missing and what ethnic groups are missing. Of the ethnic groups missing what proportion of the general

	chinese population would they be? The reviewer also provided a marked copy with additional comments. Please contact the publisher for full details.

REVIEWER	Thomas Volken Zurich University of Applied Sciences School of Health Professions Winterthur, Switzerland No Competing Interest
REVIEW RETURNED	28-Aug-2017

GENERAL COMMENTS	In their population-based cross-sectional study, the authors investigated the distribution of ABO/Rh blood groups in China. The study is based on an impressive sample of roughly 3.5 million blood samples from NFPHEP participants. Moreover, the study is well structured and clearly written. Consequently, I have only minor points which should be addressed by the authors. 1) Page 5, line 24: "(…) using data from 512 594 whole blood donations at THE five blood centres in China (…)". To make it clear to the reader that there are more than just five blood centres, the authors should drop the article, i.e. "THE". Since these five centres that were reported by Guo (2012) are compared with the authors' population-based data, it would also make sense to present the reader with the total number of blood centres in China. According to Yong-Hua Yin et al. (Blood donation in China: sustaining efforts and challenges in achieving safety and availability. Transfusion 2015; 55; 2523-2530) there seem to be 32 blood centres (Yin et al.; Table 1). 2) Page 5, line 30-32. "And our findings also reflected that individuals with blood group O might be more likely to make blood donations." It seems that the authors entirely derived this finding from comparing the percentage of O phenotype reported by Guo et al. (34%) with their population-based O phenotype (30%). However, the percentage of the Han ethnicity (whole blood) in the Guo study ranged from 67.8% to 98.7% and was 86.2% over all five centres (Guo 2012, Table 1). Clearly, the proportion of Han in these five centres was below 90.6% which may also explain why the prevalence of O phenotypes was higher in the Guo study. Consequently, the authors should either explain in more depth, why they speculated that individuals with blood type O are more inclined to give blood or they should clearly state that this is a speculation and further research is needed to substantiate this claim. 3) Page 5, lines 25-27. It is not entirely clear why the authors are referring to Apercu et al. and their study in Uganda. In order to be relevant for the discussion in the paragraph's context, the Apercu study should have compared population-based blood group O distribution (or ABO in general) with corresponding data from blood donors. However, as the authors indicated, the Apercu study included blood donors only. The authors should either delete the sentence referring to the Apercu study or provide further information on the population-based distribution of blood group O in Uganda. 4) Page 12, Figure 3. Please insert a legend that assigns colours to ethnic groups.

REVIEWER	Nicholas B. Larson Department of Health Sciences Research, Mayo Clinic, Rochester, MN United States
REVIEW RETURNED	11-Sep-2017

GENERAL COMMENTS	The authors present a cross-sectional study of ABO/Rh distributions among ethnic groups in China. The study is particularly notable for both its size and exploration within Chinese ethnic sub-populations. The methods implemented are straightforward and clearly described. Overall, the manuscript is well-written, clear, and concise. The only major limitation is its limited impact, as the study is inherently descriptive. However, discussion on distributions of "universal donor" blood types (ORh-) among the ethnicities studied clearly is useful information for, say, blood drive prioritization. One minor comment is the authors cite the blood group O proportion of “Mauritanian” to be 49.10%. The country’s name should be “Mauritania”. Additionally, Figure 2 seems a bit redundant given the complete distributional information is presented in Figure 1, and could alternatively be considered for supplementary material.

VERSION 1 – AUTHOR RESPONSE

Reviewer: 1
Reviewer Name: Paul Froom
Institution and Country: Tel Aviv University, Israel

Comment: The paper is poorly presented. There are too many tables, some redundant. why do you the aim of this study is to understand more about the ethic groups need table 1 with the demographic details (what is the relevance of proportion of farmers for example).They certainly cannot make a case for policy based on the findings. The percentages should be limited to 1 point after the decimal place for clarity. The figure 3 is mis-labled.

-Response: Thanks for the Reviewer’s suggestion. We presented socio-demographic characteristics of study population in table 1 to tell the readers about basic information of the participants included in our study. Table 1 with the demographic details is helpful for the readers to know what kind of people were included in this study. We have deleted the redundant figures (figure 2 and figure 4). And we have limited all the percentages to 1 point after the decimal place, except for the percentages of RhD- in table 3. Because the percentages of RhD- are mostly less than 1%, we thought that it would be clearer to show the percentages of RhD- in 2 decimal places in table 3. We are sorry for the mislabeled figure 3. We have added labels in the figure 3.

Reviewer: 2
Reviewer Name: Rena Hirani
Institution and Country: Australian Red Cross Blood Service

Comment: The authors have described the ethnic distribution of ABO and Rh(D) type within the general Chinese population. This study would be valuable for the Chinese blood donor organisations to understand which ethnic groups they are mostly likely to encounter and how the blood groups would form part of this diversity. Overall the standard of writing is suitable, however some suggestions

have been requested. Specific comments that need to be addressed have been annotated and attached in the file. Sections in yellow either need to be addressed, contain errors or a change has been made for the authors to consider from the original document.
Rhesus is no longer the accepted term under the ISBT guidelines. Also it should be stipulated which antigen is being analysed. Rh can refer to the D and CE systems as well as other systems. Since the CE was not analysed and can also result in Rh negative phenotypes with variable expressions in the community it should be stipulated that it was the Rh(D) group analysed. Acceptable nomenclature include RhD, Rh(D) or D. Whichever is chosen should be used consistently throughout where currently a number of them are used interchangeably. Similarly either the words 'negative' 'positive' should be used or the symbols not both.

-Response: Thanks for the Reviewer's suggestion. Following the Reviewer's suggestion, we have replaced "Rh" to "RhD" throughout the manuscript to make it consistently. And we have also replaced ' RhD negative' and ' RhD positive' to "RhD+" and "RhD-" throughout the manuscript. All the revised portions are marked in red in the revised manuscript.

Comment: In the statistics analysis of the methods the confidence intervals used were not stated.

-Response: Thanks for the Reviewer's suggestion. We have added the methods the confidence intervals in the revised manuscript. Please refer to Page 4 Line 17-22 in the statistics analysis section.

Comment: If the aim of this study is to understand more about the ethnic groups, some more information on the demographic breakdowns would be useful in the results section. Proportions of females are missing as are the ethnic group male and female breakdowns. This could be added to table 1 briefly where the male proportion can be stated in brackets where the ethnic groups are shown.

-Response: Thanks for the Reviewer's suggestion. We agree that the proportion of male and female in different ethnic group would be useful in the results. Following the Reviewer's suggestion, we have added socio-demographic characteristics of male and female respectively in the table 1. Please refer to table 1.

Comment: Table 2 and 3, the asterix for showing significance is not placed correctly. I believe the authors are trying to say that the proportion of A, B, AB and O is different between each group. i.e. are the authors trying to say that for example the difference the A blood group proportion between the Yi (33.95%) and Zhuang (25.19%) is statistically different or that for Zhuang the proportion of group O (41.81%), group B (27.49%), group A (25.19%) and group AB (5.5%) is statistically significant? For table 3 this is clearer in that the proportion of Rh(D) positive is significantly different to Rh(D) negative people in all ethnic groups. However it is clear that Uygur ethnicity is more significantly different to the other groups so perhaps the asterix should be placed next to that groups results. Comment should be made whether Yi, Han and 'others' are significantly different from each other with regard to the proportion of Rh(D) negativity.
-Response: Thanks for the Reviewer's suggestion. In table 2 of the original manuscript, we placed asterix next to blood group A was to demonstrate that the proportion of A blood group was statistically different in nine ethnic groups. Instead of describing that the distribution of ABO blood group was different in Yi and Zhuang for example, we thought that it might be more useful for readers to know which ethnic group had higher proportion of group A, group B, group O, or group AB. For example, we found that Yi ethnic group was with significantly higher proportion of A phenotype (34.0%) compared with other eight ethnic groups (all $p<0.01$). Thus, following the Reviewer's suggestions, we have placed asterix directly next to relevant proportions to make it clearer in the revised manuscript. Please refer to table 2 and table 3. In table 3, we have also added 95% CI for the proportion of RhD-. Following the Reviewer's suggestions, we compared the proportion of RhD- in Yi, Han and other

ethnic groups and found that they were all significantly different from each other (all P<0.01). And we also used logistic regression to compare the proportion of RhD- in other ethnic groups with Han ethnic group. Please refer to Page 5 Line 4-9.

Comment: Figure 1 and 2 have the same information in different graphs and i don't think they are both necessary. I think figure 1 suffices.

-Response: Thanks for the Reviewer's suggestion. We have deleted figure 2 in the revised manuscript following the Reviewer's suggestion.

Comment: Figure 3 the figure key is missing

-Response: Thanks for the Reviewer's suggestion. We are sorry for the missing figure key in the original figure 3. We have added it in the original figure 3 (figure 2 in the revised manuscript).

Comment: Figure 4 please use the same orientation and organization as used in figure 1 to prevent confusion for readers.

-Response: Thanks for the Reviewer's suggestion. If we use the same orientation and organization in figure 4 as used in figure 1, the bars of group A RhD-, B RhD-, O RhD- and AB RhD- can not be shown clearly because of their small proportion (<1%). Given that the information of figure 4 has been showed in table 4, we delete figure 4 in the revised manuscript.

Comment: The discussion needs a lot of work and is not very strongly concluding of the work conducted. The authors report the proportions of ABO and Rh(D) type for the ethnic groups but the text of putting them in context of other Asian studies or against the Caucasian populations is scattered throughout the discussion. This should be consolidated into one paragraph.

-Response: Thanks for the Reviewer's suggestion. We have revised the discussion in the revised manuscript. According to the Reviewer's suggestion, we have consolidated them into one paragraph. We have briefly reported the proportions of ABO and RhD type for the ethnic groups in one sentence in paragraph 2 (Page 5 Line 50-53) in the discussion, instead of putting them scattered.

Comment: the point of the publication from Australia on O Rh(D) negative blood use was that only a small proportion of O Rh(D) negative blood units were used in patients who required them (O Rh(D) negative recipients, trauma, obstetrics and neonates). Perhaps the authors would like to comment on that fact that since 98.98% of their population findings were Rh(D) positive individuals why this could not be applied to the blood donation sector in China. Why has the rate of O Rh(D) negative blood collections doubled from 2006 to 2012 when 98.98% of the population are Rh(D) positive. Are there plans and strategies to use the authors information to inform the clinical community of their findings and how they do not need to use O Rh(D) negative blood units.
Although the information given does not include the willingness of the participants to donate, will this information be used to target blood donors specifically?

-Response: We are sorry for placing the sentence of "In China, the whole blood collection has increased rapidly since the past decade, from 6.75 million donations in 2006 to 12.32 million donations in 2011, however, still far from the ever-increasing demand." next to the sentence of "The supply of the "universal" ORh– blood group on time and on demand to hospitals is an ongoing challenge", which may be misleading. It is the whole blood collection that doubled from 2006 to 2012, which is the total number of all kinds of blood donors, not for the rate of O RhD negative blood collections. We have moved this sentence to the appropriate paragraph. Please refer to Page 6 Line 17-20.

Group O RhD– is a precious resource that are often in short supply. In our opinion, Information on the distribution of the “universal” O RhD– blood group in different ethnic groups is of importance for developing better rational strategies for blood collection and management in China, especially during blood shortages. The proportion of group O RhD– was only 0.3% in the general population found in our study, thus it might be harder to encounter group O RhD– in Asian donors compared with Caucasian donors. However, the need for this precious resource still exists for O RhD– recipients, especially for trauma, obstetric and neonatal patients. The findings of a much higher proportion of group O RhD– in the Uygur population compared with other populations suggest that the government should make an extra effort to encourage people of the Uygur ethnicity to donate blood, especially for emergency blood supplies. Please refer to Page 6 Line 23-46.

Comment: I also did not understand the reference to blood groups and hereditary diseases as this cohort was not examined for this purpose.

-Response: We used references regarding blood groups and diseases in the discussion was to tell readers that, besides of blood collection and management, from a preventive point of view on disease, understanding the distribution of blood groups can also provide information on the potential risk of diseases for the general population.

Comment: The authors mention that they did not analyse all the ethnic minorities 'due to the lack of relative information' can the authors please state what information is missing and what ethnic groups are missing. Of the ethnic groups missing what proportion of the general chinese population would they be?

-Response: There are 56 ethnic groups in China. According to the Sixth National Population Census Report, the majority of the population in China are of Han ethnicity (91.6%) and the minority of the population are of the other 55 ethnicities (8.4%). The Zhuang, Manchu, Uygur, Miao, Yi, Hui, and Mongolian populations were assessed in our study; they are the top seven ethnic groups among the 55 minorities. In the questionnaire, ethnic groups were divided as Han, Uygur, Zhuang, Manchu, Miao, Yi, Mongolian, Hui, and Others. Thus, except for the seven ethnic groups, other ethnic groups were all in the group of “Others” and could not be further analyzed in this study. We have added a paragraph for introduction and discussion ethnicities groups in China. Please refer to Page 6 Line 12-22.

Reviewer: 3

Reviewer Name: Thomas Volken
Institution and Country: Zurich University of Applied Sciences, School of Health Professions, Winterthur, Switzerland

In their population-based cross-sectional study, the authors investigated the distribution of ABO/Rh blood groups in China. The study is based on an impressive sample of roughly 3.5 million blood samples from NFPHEP participants. Moreover, the study is well structured and clearly written. Consequently, I have only minor points which should be addressed by the authors.

1) Page 5, line 24: “(…) using data from 512 594 whole blood donations at THE five blood centres in China (…)”. To make it clear to the reader that there are more than just five blood centres, the authors should drop the article, i.e. “THE”. Since these five centres that were reported by Guo (2012) are compared with the authors’ population-based data, it would also make sense to present the reader with the total number of blood centres in China. According to Yong-Hua Yin et al. (Blood donation in China: sustaining efforts and challenges in achieving safety and availability. Transfusion 2015; 55; 2523-2530) there seem to be 32 blood centres (Yin et al.; Table 1).

-Response: Thanks for the Reviewer's suggestions. Yes, there are 32 blood centers in China. We have deleted "The" in that sentence following the Reviewer's suggestions. And we have added a sentence for presenting the reader with the total number of blood centres in China. Please refer to Page 5 Line 26-27.

2) Page 5, line 30-32. "And our findings also reflected that individuals with blood group O might be more likely to make blood donations." It seems that the authors entirely derived this finding from comparing the percentage of O phenotype reported by Guo et al. (34%) with their population-based O phenotype (30%). However, the percentage of the Han ethnicity (whole blood) in the Guo study ranged from 67.8% to 98.7% and was 86.2% over all five centres (Guo 2012, Table 1). Clearly, the proportion of Han in these five centres was below 90.6% which may also explain why the prevalence of O phenotypes was higher in the Guo study. Consequently, the authors should either explain in more depth, why they speculated that individuals with blood type O are more inclined to give blood or they should clearly state that this is a speculation and further research is needed to substantiate this claim.

-Response: Thanks for the Reviewer's suggestion. We agree that different proportions of Han ethnicity might contribute to the discrepancy. One possible reason was that the proportions of Han ethnicity were lower in blood donors (86.2%) than in the general population (>90%). The other possible reason was that those with O type blood may donate more due to being universal donors. And this needs to be further addressed in future studies. We have added it in the discussion. Please refer to Page 5 Line 40-43.

3) Page 5, lines 25-27. It is not entirely clear why the authors are referring to Apercu et al. and their study in Uganda. In order to be relevant for the discussion in the paragraph's context, the Apercu study should have compared population-based blood group O distribution (or ABO in general) with corresponding data from blood donors. However, as the authors indicated, the Apercu study included blood donors only. The authors should either delete the sentence referring to the Apercu study or provide further information on the population-based distribution of blood group O in Uganda.

-Response: Thanks for the Reviewer's suggestion. We quoted Apercu et al. and their study in Uganda was to show that the proportion of blood type O (50%) was relatively high in blood donors, compared with the results of general population in our study. We agree with the Reviewer's suggestion that we should provide further information on the population-based distribution of blood group O. However, literatures regarding ethnic diversity on blood distribution among general population were limited, most of the evidence were from blood donors, and some were from patients in the hospital. And that is the reason for us to conduct this study in the general population. This is the first epidemiology study focusing on the blood distribution among different ethnic groups in general population in China. Following the Reviewer's suggestion, we have deleted the Apercu study. And we have added a hospital-based cohort study for patients (Reference 17). Please refer to Page 5 Line 31-35.

4) Page 12, Figure 3. Please insert a legend that assigns colours to ethnic groups.

-Response: Thanks for the Reviewer's suggestion. We are sorry for the missing legend in the original figure 3. We have added it in the original figure 3 (figure 2 in the revised manuscript).

Reviewer: 4

Reviewer Name: Nicholas B. Larson
Institution and Country: Department of Health Sciences Research, Mayo Clinic, Rochester, MN United States

The authors present a cross-sectional study of ABO/Rh distributions among ethnic groups in China. The study is particularly notable for both its size and exploration within Chinese ethnic sub-populations. The methods implemented are straightforward and clearly described. Overall, the manuscript is well-written, clear, and concise. The only major limitation is its limited impact, as the study is inherently descriptive. However, discussion on distributions of "universal donor" blood types (ORh-) among the ethnicities studied clearly is useful information for, say, blood drive prioritization.

Comment: One minor comment is the authors cite the blood group O proportion of “Mauritanian” to be 49.10%. The country’s name should be “Mauritania”. Additionally, Figure 2 seems a bit redundant given the complete distributional information is presented in Figure 1, and could alternatively be considered for supplementary material.

-Response: Thanks for the Reviewer’s suggestion. We have revised it as“Mauritania”. We are sorry for the relevant redundant information showed in Figure 1 and Figure 2. We have deleted the original Figure 2 in the revised manuscript.

VERSION 2 – REVIEW

REVIEWER	Rena Hirani Australian Red Cross Blood Service
REVIEW RETURNED	09-Oct-2017

GENERAL COMMENTS	This is a much improved version of the manuscript, however there are still difficulties with the presentation of the dataset and discussion points. I have included my responses to the authors reviewer response letter to point out some identified difficulties. I have also placed the PDF version of the draft manuscript with annotations of points for the author to consider. The reviewer also provided a marked copy with additional comments. Please contact the publisher for full details.

REVIEWER	Thomas Volken Zurich University of Applied Sciences School of Health Professions CH-8401 Winterthur, Switzerland
REVIEW RETURNED	05-Oct-2017

GENERAL COMMENTS	The manuscript has been substantially improved and the authors have thoroughly addressed all issues. I have no further comments.

VERSION 2 – AUTHOR RESPONSE

Reviewer: 2
Reviewer Name: Rena Hirani
Institution and Country: Australian Red Cross Blood Service

Comment: This is a much improved version of the manuscript, however there are still difficulties with the presentation of the dataset and discussion points. I have included my responses to the authors' reviewer response letter to point out some identified difficulties. I have also placed the PDF version of the draft manuscript with annotations of points for the author to consider.

-Response: We are very grateful to the Reviewer's comments on our paper. We have revised our paper according to the Reviewer's suggestions. Here below is our description on the revision according to the comments:

1. As mentioned previously by reviewer it is not correct at all to use rhesus in the context of the Rh blood system. Rhesus is not an approved acronym or abbreviation under international standards of nomenclature for blood groups. The reference to 'rhesus' should be removed completely from this manuscript and replaced only with Rh.

-Response: Thanks for the Reviewer's suggestion. We have removed 'rhesus' completely from the revised manuscript and replaced only with Rh. Please refer to "Rh" (marked in red) the revised manuscript.

2. Please work to improve the quality of the English throughout your manuscript. I do not agree completely that this has been corrected and have pointed out passages where improvements need to be made.

-Response: Much thanks for the Reviewer's specific suggestions on improving the quality of the English in the manuscript. According to the Reviewer's suggestions, we have revised all these passages where improvements need to be made. The changes are listed below:
1) Page 13 Line 9: The repeated sentence has been deleted.
2) Page 13 Line 11: We have added the sentence for the objective of this study in the abstract.
3) Page 13 Line 14: We have added "on ABO groups and ethnicities" after the word "Data".
4) Page 14 Line 18: We have changed "while" to "whilst".
5) Page 14 Line 21: We have changed "composes" to "comprises".
6) Page 14 Line 21: We agree that the sentence "its blood supply has a potential effect on the global community" was not clear. We have deleted it. This sentence is originally from reference 8. The authors of the reference were trying to say that Chinese migrating population means this information is needed globally.
7) Page 14 Line 24: First time donors do not come back as frequent donors according to the reference. And that is why more than 60% of donors are first-time donors in China.
8) Page 15 Line 52: We have changed "In the rhesus blood system" to "In the Rh blood system".
9) Page 16 Line 8: The "RhD" are shown in a bold font in the revised manuscript.
10) Page 16 Line 22: We have added "on blood screening and supply" after the word "efforts".
11) Page 16 Line 38: We have deleted the sentence "These data differ from ours", following the Reviewer's suggestion.
12) Page 16 Line 27-52 Following the Reviewer's suggestion, we combine the papers being referenced. We have combined these discussion into one paragraph, to make the discussion clearer and concisely. In the revised version, we compare our findings with the other references in the

following order: general population in China, donors in China, and then populations outside China. Please refer to paragraph 2 in the discussion.
13) Page 17 Line 35-36: We have revised the sentence as “Understanding the distribution of blood groups in the general population can also provide information on the potential risk of diseases based on their blood groups.”

3. “Why do you the aim of this study is to understand more about the ethnic groups need table 1 with the demographic details (what is the relevance of proportion of farmers for example).They certainly cannot make a case for policy based on the findings.” The reviewer asked for justification as to why certain demographic details were included. These include education level and occupation where only farmers and workers are used. There is no definition in the methods section to what ‘worker’ means. Are they office workers, bankers, school teachers who are these ‘workers’? If they are going to include occupation and education levels they need to state why! Would this affect ability or willingness to donate blood? Would education materials need to be tailored to match the education level of each ethnicity? Comments such as these will then warrant inclusion of this data, if the data shows nothing it is also important to note this as well in the text. Furthermore the number of tables and figures still shows replication of data. Table 4 and figure 1 have exactly the same data shown as numbers or a graph. What is the value of figure 1 in addition to the table in terms of hard fact data? Similarly figure 2 is just a graphed version of a column from table 3. The data can be presented in one format but should not be replicated in two formats.

-Response: Thanks for the Reviewer’s suggestion. In this study, workers means factory workers. Office workers, bankers, teachers and traders were all in the category as “others”. We have revised this section and changed “workers” as “factory workers” to make it clearer. Please refer to table 1. It was reported that there were significant demographic variations on the donation rate (Transfus Med. 2007 Apr;17(2):83-7.). Data from China donors also showed that blood donors in China were predominantly male workers (means factory workers), farmers, and students between the ages of 18 and 45 (Transfusion, 2015, 55 (10) :2523-30). Demographic details is useful for the readers because it would affect willingness to donate blood. And education materials had impact on nondonors' willingness to donate blood (Transfusion. 2016 Dec;56(12):2995-3003.). We agree with the Reviewer’s opinion that education materials need to be tailored to match the education level of each ethnicity. Given the above reasons, we think it would be better to keep the demographic details in the table 1. We agree that there is no need to show figure 1 and 2, because the tables have shown hard fact data. To avoid replication on the tables and figures, we delete the figure 1 and 2 in the revised manuscript.

4. For the column labelled ‘proportion’ the addition of confidence intervals has improved the data. However the odds ratio column should be removed as this detracts from the message of the table.

-Response: Thanks for the Reviewer’s suggestion. We have removed the odds ratio column in table 3. Please refer to table 3.

5. This comment has been addressed appropriately in table 1. However the percentages displayed are not useful. It would be a better addition the propotion of males and females of the total number of people analysed per ethnicity is used throughout the various rows in the table. i.e. 90.6% of people are Han the % of males should be shown which is 48.9% and females which is 51.1%. the relevance of having higher female population in some ethnicities over others may influence which donors are approached. Male donors are preferred due to reduced risk of transfusion related acute lung injury from male derived products.

-Response: Thanks for the Reviewer's suggestion. We agree that it would be better to revise the way percentages are presented. We have revised the proportions as the proportion of males and females of the total number of people analyzed per ethnicity in table 1. Please refer to table 1.

6. Interestingly the data presented indicates that 98.98% of the population is Rh(D)+, therefore identifying ethnicities with higher O D- is of relevance. However if 98.98% of the population is Rh(D)+, the likelihood of emergency/trauma patients being Rh(D)- and therefore susceptible to alloimmunisation are so remote that collections of O Rh(D)+ seems more sensible. Perhaps this should be discussed both domestically and in the international context. China perhaps has a more enviable position where Rh(D)- blood types may not be as vitally required. Arguments of Rh(D)- blood types for emergency use are common, however I refer you to following references indicating likelihood of forming D antibodies after transfusion of Rh(D)+ blood into Rh(D)- individuals.
Selleng et al Lancet Haematol 4(5) e218-e224 2017
Meyer et al Transfusion 55(4):791-795 2015
Discussion points around this can make this ethic ABO group dissection really relevant to the trauma and medicine field in China.

-Response: Thanks for the Reviewer's suggestion. We have revised the discussion according to the Reviewer's suggestion. And we have added these two references in the discussion. Please refer to Page 17 Line 21-30.

Thanks again for the Reviewer's professional and specific comments on improving our manuscript.

Reviewer: 3
Reviewer Name: Thomas Volken
Institution and Country: Zurich University of Applied Sciences, School of Health Professions, CH-8401 Winterthur, Switzerland

Comment: The manuscript has been substantially improved and the authors have thoroughly addressed all issues. I have no further comments.

-Response: Thanks again for the Reviewer's comments and suggestions on our paper.

VERSION 3 – REVIEW

REVIEWER	Rena Hirani Australian Red Cross Blood Service
REVIEW RETURNED	18-Oct-2017

GENERAL COMMENTS	Very minor changes to tables and text added. No requirement for revision once these changes have been made. The reviewer also provided a marked copy with additional comments. Please contact the publisher for full details.